



SEQUENCE LISTING

<110> CASTILLO, GERARDO M.
NGUYEN, BETH P.
LAKE, THOMAS P.
SNOW, ALAN D.

<120> SMALL PEPTIDES FOR THE TREATMENT OF ALZHEIMER'S DISEASE
AND OTHER BETA-AMYLOID PROTEIN FIBRILLOGENESIS
DISORDERS

<130> PROTEO.P03CI2

<140> 10/821,250

<141> 2004-04-08

<150> 60/461,655

<151> 2003-04-08

<150> 09/962,955

<151> 2001-09-24

<150> 09/938,275

<151> 2001-08-22

<150> 08/947,057

<151> 1997-10-08

<160> 108

<170> PatentIn Ver. 3.2

<210> 1

<211> 12

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic
peptide

<400> 1

Arg Lys Arg Leu Gln Val Gln Leu Ser Ile Arg Thr
1 5 10

<210> 2

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 2

Lys Ala Phe Asp Ile Thr Tyr Val Arg Leu Lys Phe
1 5 10

<210> 3
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<212> PRT
<213> Artificial Sequence

<220>
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Arg Gln Val Phe Gln Val Ala Tyr Ile Ile Ile Lys Ala
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His Gln Thr Trp Thr Arg Asn Leu Gln Val Thr Leu
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<220>
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Ile Ser Asn Val Phe Val Gln Arg Leu Ser Leu Ser
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<210> 6
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Ala Ser Pro Pro Ser Val Lys Val Trp Gln Asp Ala
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<210> 7
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<212> PRT
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<220>
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<400> 7
Arg Gly Leu Val Phe His Thr Gly Thr Lys Asn Ser Phe
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<210> 8
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<400> 8
Tyr Leu Ser Lys Gly Arg Leu Val Phe Ala Leu Gly
1 5 10

<210> 9
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<212> PRT
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Asn Asp Gly Lys Trp His Thr Val Val Phe Gly His
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<400> 10
Gly Asn Ser Thr Ile Ser Ile Arg Ala Pro Val Tyr
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<400> 11

Thr Leu Phe Leu Ala His Gly Arg Leu Val Phe Met
1 5 10

<210> 12
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<400> 12
His Pro Asp Asp Phe Val Phe Tyr Val Gly Gly Tyr
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<210> 13
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<220>
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<400> 13
Trp Leu Tyr Val Asp Asp Gln Leu Gln Leu Val Lys
1 5 10

<210> 14
<211> 12
<212> PRT
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<400> 14
Val Gln Ser Arg Gln His Ser Arg Ala Gly Gln Trp
1 5 10

<210> 15
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<400> 15
Ala Gly Gln Trp His Arg Val Ser Val Arg Trp Gly
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<210> 16

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<400> 16
Val Arg Trp Gly Met Gln Gln Ile Gln Leu Val Val
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<210> 17
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Thr Trp Ser Gln Lys Ala Leu His His Arg Val Pro
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Asp Gly Arg Trp His Arg Val Ala Val Ile Met Gly
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<223> Description of Artificial Sequence: Synthetic peptide

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Lys Pro Arg Leu Gln Phe Ser Leu Asp Ile Gln Thr
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<210> 21

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<210> 22

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<210> 27
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<400> 27
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<210> 28
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<220>
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<400> 28
 Phe Leu Pro Leu Ala Leu Pro Asp Val Ala Pro Ile
 1 5 10

<210> 29
 <211> 12

<212> PRT
<213> Artificial Sequence

<220>
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<400> 29
Gly Pro Leu Pro Ser Tyr Leu Gln Phe Val Gly Ile
1 5 10

<210> 30
<211> 12
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Ser Val Gln Ile Gln Gly Ala Val Gly Met Arg Gly
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<210> 31
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<213> Homo sapiens

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Asp Trp Lys Leu Val Arg Ser Ala Ser Phe Ser Arg Gly Gly Gln Leu
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Ser Phe Thr Asp Leu Gly Leu Pro Pro Thr Asp His Leu Gln Ala Ser
35 40 45

Phe Gly Phe Gln Thr Phe Gln Pro Ser Gly Ile Leu Leu Asp His Gln
50 55 60

Thr Trp Thr Arg Asn Leu Gln Val Thr Leu Glu Asp Gly Tyr Ile Glu
65 70 75 80

Leu Ser Thr Ser Asp Ser Gly Gly Pro Ile Phe Lys Ser Pro Gln Thr
85 90 95

Tyr Met Asp Gly Leu Leu His Tyr Val Ser Val Ile Ser Asp Asn Ser
100 105 110

Gly Leu Arg Leu Leu Ile Asp Asp Gln Leu Leu Arg Asn Ser Lys Arg
115 120 125

Leu Lys His Ile Ser Ser Ser Arg Gln Ser Leu Arg Leu Gly Gly Ser
130 135 140

Asn Phe Glu Gly Cys Ile Ser Asn Val Phe Val Gln Arg Leu Ser Leu
145 150 155 160

Ser Pro Glu Val Leu Asp Leu Thr Ser Asn Ser Leu Lys Arg Asp Val
 165 170 175
 Ser Leu Gly Gly Cys Ser Leu Asn Lys Pro Pro Phe Leu Met Leu Leu
 180 185 190
 Lys Gly Ser Thr Arg Phe Asn Lys Thr Lys Thr Phe Arg Ile Asn Gln
 195 200 205
 Leu Leu Gln Asp Thr Pro Val Ala Ser Pro Arg Ser Val Lys Val Trp
 210 215 220
 Gln Asp Ala Cys Ser Pro Leu Pro Lys Thr Gln Ala Asn His Gly Ala
 225 230 235 240
 Leu Gln Phe Gly Asp Ile Pro Thr Ser His Leu Leu Phe Lys Leu Pro
 245 250 255
 Gln Glu Leu Leu Lys Pro Arg Ser Gln Phe Ala Val Asp Met Gln Thr
 260 265 270
 Thr Ser Ser Arg Gly Leu Val Phe His Thr Gly Thr Lys Asn Ser Phe
 275 280 285
 Met Ala Leu Tyr Leu Ser Lys Gly Arg Leu Val Phe Ala Leu Gly Thr
 290 295 300
 Asp Gly Lys Lys Leu Arg Ile Lys Ser Lys Glu Lys Cys Asn Asp Gly
 305 310 315 320
 Lys Trp His Thr Val Val Phe Gly His Asp Gly Glu Lys Gly Arg Leu
 325 330 335
 Val Val Asp Gly Leu Arg Ala Arg Glu Gly Ser Leu Pro Gly Asn Ser
 340 345 350
 Thr Ile Ser Ile Arg Ala Pro Val Tyr Leu Gly Ser Pro Pro Ser Gly
 355 360 365
 Lys Pro Lys Ser Leu Pro Thr Asn Ser Phe Val Gly Cys Leu Lys Asn
 370 375 380
 Phe Gln Leu Asp Ser Lys Pro Leu Tyr Thr Pro Ser Ser Ser Phe Gly
 385 390 395 400
 Val Ser Ser Cys Leu Gly Gly Pro Leu Glu Lys Gly Ile Tyr Phe Ser
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<210> 32
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 20 25 30

Ala Lys Lys Glu Tyr Met Gly Leu Ala Ile Lys Asn Asp Asn Leu Val
 35 40 45
 Tyr Val Tyr Asn Leu Gly Met Lys Asp Val Glu Ile Leu Leu Asp Ser
 50 55 60
 Lys Pro Val Ser Ser Trp Pro Ala Tyr Phe Ser Ile Val Lys Ile Glu
 65 70 75 80
 Arg Val Gly Lys His Gly Lys Val Phe Leu Thr Val Pro Ser Ser Ser
 85 90 95
 Ser Thr Ala Glu Glu Lys Phe Ile Lys Lys Gly Glu Phe Ala Gly Asp
 100 105 110
 Asp Ser Leu Leu Asp Leu Thr Pro Glu Asp Thr Val Phe Tyr Val Gly
 115 120 125
 Gly Val Pro Ala Asn Phe Lys Leu Pro Ala Ser Leu Asn Leu Pro Ser
 130 135 140
 Tyr Ser Gly Cys Leu Glu Leu Ala Thr Leu Asn Asn Asp Val Ile Ser
 145 150 155 160
 Leu Tyr Asn Phe Lys His Ile Tyr Asn Met Asp Pro Ser Lys Ser Val
 165 170 175
 Pro Cys Ala Arg Asp Lys Leu Ala Phe Thr Gln Ser Arg Ala Ala Ser
 180 185 190
 Tyr Phe Phe Asp Gly Ser Ser Tyr Ala Val Val Arg Asp Ile Thr Arg
 195 200 205
 Arg Gly Lys Phe Gly Gln Val Thr Arg Phe Asp Ile Glu Ile Arg Thr
 210 215 220
 Pro Ala Asp Asn Gly Leu Val Leu Leu Met Val Asn Gly Ser Met Phe
 225 230 235 240
 Phe Ser Leu Glu Met Arg Asn Gly Tyr Leu His Val Phe Tyr Asp Phe
 245 250 255
 Gly Phe Ser Asn Gly Pro Val His Leu Glu Asp Thr Leu Lys Lys Ala
 260 265 270
 Gln Ile Asn Asp Ala Lys Tyr Arg Glu Ile Ser Ile Ile Tyr His Asn
 275 280 285
 Asp Lys Lys Met Ile Leu Val Val Asp Arg Arg His Val Lys Ser Thr
 290 295 300
 Asp Asn Glu Lys Lys Lys Ile Pro Phe Thr Asp Ile Tyr Ile Gly Gly
 305 310 315 320
 Ala Pro Gln Glu Val Leu Gln Ser Arg Thr Leu Arg Ala His Leu Pro
 325 330 335
 Leu Asp Ile Asn Phe Arg Gly Cys Met Lys Gly Ile Gln Phe Gln Lys
 340 345 350
 Lys Asp Phe Asn Leu Leu Glu Gln Thr Glu Thr Leu Gly Val Gly Tyr

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Gly	Cys	Pro	Glu	Asp	Ser	Leu	Ile	Ser	Arg	Arg	Ala	Tyr	Phe	Asn	Gly
370						375					380				
Gln	Ser	Phe	Ile	Ala	Ser	Ile	Gln	Lys	Ile	Ser	Phe	Phe	Asp	Gly	Phe
385					390					395					400
Glu	Gly	Gly	Phe	Asn	Phe	Arg	Thr	Leu	Gln	Pro	Asn	Gly	Leu	Leu	Phe
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Tyr	Tyr	Thr	Ser	Gly	Ser	Asp	Val	Phe	Ser	Ile	Ser	Leu	Asp	Asn	Gly
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Thr	Val	Val	Met	Asp	Val	Lys	Gly	Ile	Lys	Val	Met	Ser	Thr	Asp	Lys
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Gln	Tyr	His	Asp	Gly	Leu	Pro	His	Phe	Val	Val	Thr	Ser	Ile	Ser	Asp
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Thr	Arg	Tyr	Glu	Leu	Val	Val	Asp	Lys	Ser	Arg	Leu	Arg	Gly	Lys	Asn
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Pro	Thr	Lys	Gly	Lys	Ala	Glu	Gln	Thr	Gln	Thr	Thr	Glu	Lys	Lys	Phe
				485					490					495	
Tyr	Phe	Gly	Gly	Ser	Pro	Ile	Ser	Pro	Gln	Tyr	Ala	Asn	Phe	Thr	Gly
			500					505					510		
Cys	Ile	Ser	Asn	Ala	Tyr	Phe	Thr	Arg	Leu	Asp	Arg	Asp	Val	Glu	Val
		515					520					525			
Glu	Ala	Phe	Gln	Arg	Tyr	Ser	Glu	Lys	Val	His	Thr	Ser	Leu	Tyr	Glu
	530					535					540				
Cys	Pro	Ile	Glu	Ser	Ser	Pro	Leu	Phe	Leu	Leu	His	Lys	Lys	Gly	Lys
545					550					555					560
Asn	Ser	Ser	Lys	Pro	Lys	Thr	Asn	Lys	Gln	Gly	Glu	Lys	Ser	Lys	Asp
				565					570					575	
Ala	Pro	Ser	Trp	Asp	Pro	Ile	Gly	Leu	Lys	Phe	Leu	Glu	Gln	Lys	Ala
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Pro	Arg	Asp	Ser	His	Cys	His	Leu	Phe	Ser	Ser	Pro	Arg	Ala	Ile	Glu
		595					600					605			
His	Ala	Tyr	Gln	Tyr	Gly	Gly	Thr	Ala	Asn	Ser	Arg	Gln	Glu	Phe	Glu
	610					615					620				
His	Glu	Gln	Gly	Asp	Phe	Gly	Glu	Lys	Ser	Gln	Phe	Ser	Ile	Arg	Leu
625						630					635				640
Lys	Thr	Arg	Ser	Ser	His	Gly	Met	Ile	Phe	Tyr	Val	Ser	Asp	Gln	Glu
				645					650					655	
Glu	Asn	Asp	Phe	Met	Thr	Leu	Phe	Leu	Ala	His	Gly	Arg	Leu	Val	Phe
			660				665						670		
Met	Phe	Asn	Val	Gly	His	Lys	Lys	Leu	Lys	Ile	Arg	Ser	Gln	Glu	Lys
		675					680					685			

Tyr Asn Asp Gly Leu Trp His Asp Val Ile Phe Ile Arg Glu Lys Ser
 690 695 700
 Ser Gly Arg Leu Val Ile Asp Gly Leu Arg Val Leu Glu Glu Arg Leu
 705 710 715 720
 Pro Pro Ser Gly Ala Ala Trp Lys Ile Lys Gly Pro Ile Tyr Leu Gly
 725 730 735
 Gly Val Ala Pro Gly Arg Ala Val Lys Asn Val Gln Ile Thr Ser Val
 740 745 750
 Tyr Ser Phe Ser Gly Cys Leu Gly Asn Leu Gln Leu Asn Gly Ala Ser
 755 760 765
 Ile Thr Ser Ala Ser Gln Thr Phe Ser Val Thr Pro Cys Phe Glu Gly
 770 775 780
 Pro Met Glu Thr Gly Thr Tyr Phe Ser Thr Glu Gly Gly Tyr Val Val
 785 790 795 800
 Leu Asp Glu Ser Phe Asn Ile Gly Leu Lys Phe Glu Ile Ala Phe Glu
 805 810 815
 Val Arg Pro Arg Ser Ser Ser Gly Thr Leu Val His Gly His Ser Val
 820 825 830
 Asn Gly Glu Tyr Leu Asn Val His Met Arg Asn Gly Gln Val Ile Val
 835 840 845
 Lys Val Asn Asn Gly Val Arg Asp Phe Ser Thr Ser Val Thr Pro Lys
 850 855 860
 Gln Asn Leu Cys Asp Gly Arg Trp His Arg Ile Thr Val Ile Arg Asp
 865 870 875 880
 Ser Asn Val Val Gln Leu Asp Val Asp Ser Glu Val Asn His Val Val
 885 890 895
 Gly Pro Leu Asn Pro Lys Pro Val Asp His Arg Glu Pro Val Phe Val
 900 905 910
 Gly Gly Val Pro Glu Ser Leu Leu Thr Pro Arg Leu Ala Pro Ser Lys
 915 920 925
 Pro Phe Thr Gly Cys Ile Arg His Phe Val Ile Asp Ser Arg Pro Val
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 Ser Phe Ser Lys Ala Ala Leu Val Ser Gly Ala Val Ser Ile Asn Ser
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Cys Pro Thr Ala

<210> 33
 <211> 956
 <212> PRT
 <213> Mus musculus

<400> 33

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Ala	Thr	Gly	Asp	Tyr	Met	Gly	Val	Ser	Leu	Arg	Asn	Gln	Lys	Val	His	35	40	45	
Trp	Val	Tyr	Arg	Leu	Gly	Lys	Ala	Gly	Pro	Thr	Thr	Leu	Ser	Ile	Asp	50	55	60	
Glu	Asn	Ile	Gly	Glu	Gln	Phe	Ala	Ala	Val	Ser	Ile	Asp	Arg	Thr	Leu	65	70	75	80
Gln	Phe	Gly	His	Met	Ser	Val	Thr	Val	Glu	Lys	Gln	Met	Val	His	Glu	85	90	95	
Ile	Lys	Gly	Asp	Thr	Val	Ala	Pro	Gly	Ser	Glu	Gly	Leu	Leu	Asn	Leu	100	105	110	
His	Pro	Asp	Asp	Phe	Val	Phe	Tyr	Val	Gly	Gly	Tyr	Pro	Ser	Asn	Phe	115	120	125	
Thr	Pro	Pro	Glu	Pro	Leu	Arg	Phe	Pro	Gly	Tyr	Leu	Gly	Cys	Ile	Glu	130	135	140	
Met	Glu	Thr	Leu	Asn	Glu	Glu	Val	Val	Ser	Leu	Tyr	Asn	Phe	Glu	Gln	145	150	155	160
Thr	Phe	Met	Leu	Asp	Thr	Ala	Val	Asp	Lys	Pro	Cys	Ala	Arg	Ser	Lys	165	170	175	
Ala	Thr	Gly	Asp	Pro	Trp	Leu	Thr	Asp	Gly	Ser	Tyr	Leu	Asp	Gly	Ser	180	185	190	
Gly	Phe	Ala	Arg	Ile	Ser	Phe	Glu	Lys	Gln	Phe	Ser	Asn	Thr	Lys	Arg	195	200	205	
Phe	Asp	Gln	Glu	Leu	Arg	Leu	Val	Ser	Tyr	Asn	Gly	Ile	Ile	Phe	Phe	210	215	220	
Leu	Lys	Gln	Glu	Ser	Gln	Phe	Leu	Cys	Leu	Ala	Val	Gln	Glu	Gly	Thr	225	230	235	240
Leu	Val	Leu	Phe	Tyr	Asp	Phe	Gly	Ser	Gly	Leu	Lys	Lys	Ala	Asp	Pro	245	250	255	
Leu	Gln	Pro	Pro	Gln	Ala	Leu	Thr	Ala	Ala	Ser	Lys	Ala	Ile	Gln	Val	260	265	270	
Phe	Leu	Leu	Ala	Gly	Asn	Arg	Lys	Arg	Val	Leu	Val	Arg	Val	Glu	Arg	275	280	285	
Ala	Thr	Val	Phe	Ser	Val	Asp	Gln	Asp	Asn	Met	Leu	Glu	Met	Ala	Asp	290	295	300	
Ala	Tyr	Tyr	Leu	Gly	Gly	Val	Pro	Pro	Glu	Gln	Leu	Pro	Leu	Ser	Leu	305	310	315	320
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325										330					335				
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Pro	Ile	Thr	Glu	Val	Val	Tyr	Ser	Gly	Phe	Gly	Phe	Arg	Gly	Thr	Gln				
385					390					395					400				
Asp	Asn	Asn	Leu	Leu	Tyr	Tyr	Arg	Thr	Ser	Pro	Asp	Gly	Pro	Tyr	Gln				
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Val	Ser	Leu	Arg	Glu	Gly	His	Val	Thr	Leu	Arg	Phe	Met	Asn	Gln	Glu				
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Val	Glu	Thr	Gln	Arg	Val	Phe	Ala	Asp	Gly	Ala	Pro	His	Tyr	Val	Ala				
		435					440					445							
Phe	Tyr	Ser	Asn	Val	Thr	Gly	Val	Trp	Leu	Tyr	Val	Asp	Asp	Gln	Leu				
	450					455					460								
Gln	Leu	Val	Lys	Ser	His	Glu	Arg	Thr	Thr	Pro	Met	Leu	Gln	Leu	Gln				
465					470					475					480				
Pro	Glu	Glu	Pro	Ser	Arg	Leu	Leu	Leu	Gly	Gly	Leu	Pro	Val	Ser	Gly				
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Thr	Phe	His	Asn	Phe	Ser	Gly	Cys	Ile	Ser	Asn	Val	Phe	Val	Gln	Arg				
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Leu	Arg	Gly	Pro	Gln	Arg	Val	Phe	Asp	Leu	His	Gln	Asn	Met	Gly	Ser				
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Val	Asn	Val	Ser	Val	Gly	Cys	Thr	Pro	Ala	Gln	Leu	Ile	Glu	Thr	Ser				
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Arg	Ala	Thr	Ala	Gln	Lys	Val	Ser	Arg	Arg	Ser	Arg	Gln	Pro	Ser	Gln				
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Asp	Leu	Ala	Cys	Thr	Thr	Pro	Trp	Leu	Pro	Gly	Thr	Ile	Gln	Asp	Ala				
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Tyr	Gln	Phe	Gly	Gly	Pro	Leu	Pro	Ser	Tyr	Leu	Gln	Phe	Val	Gly	Ile				
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Ser	Pro	Ser	His	Arg	Asn	Arg	Leu	His	Leu	Ser	Met	Leu	Val	Arg	Pro				
		595					600					605							
His	Ala	Ala	Ser	Gln	Gly	Leu	Leu	Leu	Ser	Thr	Ala	Pro	Met	Ser	Gly				
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Arg	Ser	Pro	Ser	Leu	Val	Leu	Phe	Leu	Asn	His	Gly	His	Phe	Val	Ala				
625					630					635					640				
Gln	Thr	Glu	Gly	Pro	Gly	Pro	Arg	Leu	Gln	Val	Gln	Ser	Arg	Gln	His				
			645						650					655					

Ser Arg Ala Gly Gln Trp His Arg Val Ser Val Arg Trp Gly Met Gln
 660 665 670
 Gln Ile Gln Leu Val Val Asp Gly Ser Gln Thr Trp Ser Gln Lys Ala
 675 680 685
 Leu His His Arg Val Pro Arg Ala Glu Arg Pro Gln Pro Tyr Thr Leu
 690 695 700
 Ser Val Gly Gly Leu Pro Ala Ser Ser Tyr Ser Ser Lys Leu Pro Val
 705 710 715 720
 Ser Val Gly Phe Ser Gly Cys Leu Lys Lys Leu Gln Leu Asp Lys Gln
 725 730 735
 Pro Leu Arg Thr Pro Thr Gln Met Val Gly Val Thr Pro Cys Val Ser
 740 745 750
 Gly Pro Leu Glu Asp Gly Leu Phe Phe Pro Gly Ser Glu Gly Val Val
 755 760 765
 Thr Leu Glu Leu Pro Lys Ala Lys Met Pro Tyr Val Ser Leu Glu Leu
 770 775 780
 Glu Met Arg Pro Leu Ala Ala Ala Gly Leu Ile Phe His Leu Gly Gln
 785 790 795 800
 Ala Leu Ala Thr Pro Tyr Met Gln Leu Lys Val Leu Thr Glu Gln Val
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 Tyr Pro Lys Leu Cys Asp Gly Arg Trp His Arg Val Ala Val Ile Met
 835 840 845
 Gly Arg Asp Thr Leu Arg Leu Glu Val Asp Thr Gln Ser Asn His Thr
 850 855 860
 Thr Gly Arg Leu Pro Glu Ser Leu Ala Gly Ser Pro Ala Leu Leu His
 865 870 875 880
 Leu Gly Ser Leu Pro Lys Ser Ser Thr Ala Arg Pro Glu Leu Pro Ala
 885 890 895
 Tyr Arg Gly Cys Leu Arg Lys Leu Leu Ile Asn Gly Ala Pro Val Asn
 900 905 910
 Val Thr Ala Ser Val Gln Ile Gln Gly Ala Val Gly Met Arg Gly Cys
 915 920 925
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